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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,291	10/28/2003	Hua Tang	TPIP021	3947

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EXAMINER	
LEWIS, AMY A	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
12/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/695,291	TANG ET AL.	
	Examiner	Art Unit	
	Amy A. Lewis	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the appeal brief filed on 7/16/2008, PROSECUTION IS HEREBY REOPENED. The following new/modified rejections are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614.

Applicants' arguments, filed 7/16/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1-8 and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirejovsky et al. (U.S. Patent No. 6,147,122), in view of Erdelmeier et al. (U.S. Patent Appl. Pub. No. 2002/0031560).

Mirejovsky et al. teach a pharmaceutical oil-in-water emulsion composition of propofol for parenteral administration which is an oil-in-water emulsion, containing sulfite as an anti-microbial agent sufficient to prevent significant growth of microorganisms (see abstract). The

reference states that one of the key requirements to the preservative containing formulation is the stabilization of the emulsion (see col. 3, lines 25-35, part e).

The propofol composition of Mirejovsky et al. is prepared by injection (column 12, line 43). Propofol is 1% by weight of the composition and is soluble in the aqueous phase (column 4, line 35; and column 3, line 27). The propofol composition also contains a water-immiscible solvent, such as vegetable oil, at 10% weight, a surfactant, such as egg or soy phosphatides, at 1.2% weight, and is formulated with pH in the range of about 4.5 to about 6.4 (column 4, lines 32-35, 48-50, 59, and 63-65; column 5, lines 19-20; and column 12, line 47).

The anti-microbial agent of the propofol composition is about 0.0075% to about 0.66% weight (column 4, lines 12-14). The anti-microbial agent is in an amount sufficient to prevent the growth, or prevent no more than a 10-fold increase in growth, of each of *S. aureus* (ATCC 6583), *E. coli* (ATCC 8739), *P. aeruginosa* (ATCC 9027), and *C. albicans* (ATCC 10231) for at least 24 hours wherein each organism is added at 50-200 colony forming units and incubated at 30-35^{0}C (column 8, 3. Microbiological activity; and column 12, lines 25-38).

Mirejovsky et al. do not teach inclusion of cysteine in the propofol formulation.

Erdelmeier et al. teach pharmaceutical compositions stabilized against decomposition or degradation with cysteine (see: abstract; para. [0017]; claims 1, 3-5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include cysteine in the propofol composition of Mirejovsky et al., having been taught that cysteine is a useful stabilizing agent in pharmaceutical compositions and motivated by the desire to increase the stability of the propofol formulation, as specifically expressed by Mirejovsky et al.

2) Claims 1-8 and 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirejovsky et al. (U.S. Patent No. 6,147,122), in view of Erdelmeier et al. (U.S. Patent Appl. Pub. No. 2002/0031560), and further in view of Mishra et al. (US 7,097,849).

Mirejovsky et al. and Erdelmeier et al. are applied as above. Neither teach inclusion of a local anesthetic in the formulation.

Mishra et al. teach a propofol composition comprising an anti-microbial agent and a local or long lasting anesthetic, such as lidocaine (column 1, line 7; and column 5, lines 47-51). Mishra et al. teach that irritation and pain upon administration is a continued problem with propofol formulations. (See: abstract, col. 3, lines 35-48).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include a local anesthetic in a propofol formulation, especially an oil in water emulsion formulation, having been taught that it is known to include anesthetic agents in such propofol formulations and motivated by the desire to reduce the pain and irritation upon administration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2) Claim(s) 3 is(are) rejected under 35 U.S.C. § 112, first paragraph, as containing subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals, such as the excipients listed in claim 4 or at page 3 of the specification, which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claim(s) 3 is(are) directed to "a GRAS excipient", which is only mentioned in the specification at page 3, but not further defined. The specification only lists examples of excipients, but does not describe how they meet the definition of being a "GRAS excipeint" or any relationship thereto.

"GRAS excipients" fail to meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus of excipients encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmacentical Co. Ltd.,* 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.Finally, *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the above chemically structurally defined chemicals (excipeints), but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3) Claims 1-8 and 10-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3, 18-50 of copending Application No. 10/677747, in view of Erdelmeier et al. (U.S. Patent Appl. Pub. No. 2002/0031560), and further in view of Mishra et al. (US 7,097,849).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both teach a pharmaceutical composition containing propofol and overlapping excipients.

Erdelmeier et al. teach pharmaceutical compositions stabilized against decomposition or degradation with cysteine (see: abstract; para. [0017]; claims 1, 3-5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include cysteine in the propofol composition, having been taught that cysteine is a useful stabilizing agent in pharmaceutical compositions and motivated by the desire to increase the stability of the propofol formulation.

Mishra et al. teach a propofol composition comprising an anti-microbial agent and a local or long lasting anesthetic, such as lidocaine (column 1, line 7; and column 5, lines 47-51). Mishra et al. teach that irritation and pain upon administration is a continued problem with propofol formulations. (See: abstract, col. 3, lines 35-48).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include a local anesthetic in a propofol formulation, especially an oil in water emulsion formulation, having been taught that it is known to include anesthetic agents in such

propofol formulations and motivated by the desire to reduce the pain and irritation upon administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4) Claims 1-8 and 10-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 8-12, 25-27 of copending Application No. 10/629308, in view of Erdelmeier et al. (U.S. Patent Appl. Pub. No. 2002/0031560).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both teach a pharmaceutical composition containing propofol, a local anesthetic, and overlapping excipients.

Erdelmeier et al. teach pharmaceutical compositions stabilized against decomposition or degradation with cysteine (see: abstract; para. [0017]; claims 1, 3-5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include cysteine in the propofol composition, having been taught that cysteine is a useful stabilizing agent in pharmaceutical compositions and motivated by the desire to increase the stability of the propofol formulation.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5) Claims 1-8 and 10-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 12, 20, 23, 25-37, 39-64,

66-68, and 71-78 of copending Application No. 10/766631, in view of Erdelmeier et al. (U.S. Patent Appl. Pub. No. 2002/0031560), and further in view of Mishra et al. (US 7,097,849).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both teach a pharmaceutical composition containing propofol and overlapping excipients.

Erdelmeier et al. teach pharmaceutical compositions stabilized against decomposition or degradation with cysteine (see: abstract; para. [0017]; claims 1, 3-5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include cysteine in the propofol composition, having been taught that cysteine is a useful stabilizing agent in pharmaceutical compositions and motivated by the desire to increase the stability of the propofol formulation.

Mishra et al. teach a propofol composition comprising an anti-microbial agent and a local or long lasting anesthetic, such as lidocaine (column 1, line 7; and column 5, lines 47-51). Mishra et al. teach that irritation and pain upon administration is a continued problem with propofol formulations. (See: abstract, col. 3, lines 35-48).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include a local anesthetic in a propofol formulation, especially an oil in water emulsion formulation, having been taught that it is known to include anesthetic agents in such propofol formulations and motivated by the desire to reduce the pain and irritation upon administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy A. Lewis whose telephone number is 571-272-9032. The examiner can normally be reached on Monday-Friday 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amy A Lewis/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614